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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,495	01/13/2005	Gerard O'Beirne	PA0248	2631

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EXAMINER	
LIU, SUE XU	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,495	O'BEIRNE ET AL.	
	Examiner	Art Unit	
	SUE LIU	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *5 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-12 and 14-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claim 20 has been cancelled as filed on 2/6/08.

Claims 1-19 are currently pending.

Claims 5 and 13 have been withdrawn.

Claims 1-4, 6-12 and 14-19 are being examined in this application.

Election/Restrictions

2. Applicant's election without traverse of the following species:

A.) DNA as the "effector nucleic acid";

B.) Fluorescent protein as the "detectable label";

C.) Organic compound as the "modulator";

in the reply filed on 2/6/08 is acknowledged. Accordingly, Claims 5 and 13 are withdrawn due to non-elected species.

Priority

3. This application is filed under 35 U.S.C 371 of PCT/GB03/02983 (filed on 7/10/03).

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers (UK 0216674.2 filed 07/18/02) have been placed of record in the file.

Information Disclosure Statement

5. The IDS filed on 1/13/05 has been considered. See the attached PTO 1449 form.

Specification

6. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. MPEP 608.01.

Claim Rejections - 35 USC § 112

Second paragraph of 35 U.S.C. 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-4, 6-12 and 14-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 recite "chemical modulators having known and unknown function", which is unclear. It is not clear what "chemical modulators" are encompassed by the claim language of "known and unknown function". It is not clear to which "function" the claim language is referring.

Claims 1 and 2 also recites "determining the distribution of an indicator nucleic acid sequence… in the presence and the absence of a first chemical modulator", which recitation is unclear and confusing. The said claim language seems to recite that the "first chemical modulator" is both "present and absent" at the same time. However, it is not clear how the "first chemical modulator" can be both "present and absent" at the same time.

Claims 1 and 2 recite "analyzing the distribution data from all combinations of said effector…" which is unclear. The instant claims 1 and 2 recite "the distribution of an indicator" in step i) of the claims. It is not clear if "the distribution data" recited in step ii) of the instant claim 1 and step iii) of the instant claim 2 is referring to the "distribution of an indicator" recited in step i). In addition, it is not clear if the said recitation in step ii) or iii) of claims 1 and 2 are referring to the distribution of the indicator or if it is referring to distribution data of all of the listed components (including the effector, modulator, indicator, etc.). Thus, one of ordinary skill in the art would not be able to apprise the metes and bounds of the instant claimed invention.

Claim 14 recites the limitation "the modulator" in line 1. There is insufficient antecedent basis for this limitation in the claim. The instant claim 1 (from which claim 14 depends) recites "a first chemical modulator" and "a second chemical modulator". It is not clear to which "modulator" the said term of the instant claim 14 is referring.

Claim 15 recites the limitation "the modulator" in line 1. There is insufficient antecedent basis for this limitation in the claim. The instant claim 1 (from which claim 15 depends) recites "a first chemical modulator" and "a second chemical modulator". It is not clear to which "modulator" the said term of the instant claim 15 is referring.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Thastrup

10. Claims **1-4, 6-11** and **14-19** are rejected under **35 U.S.C. 102(b)** as being anticipated by **Thastrup** et al (WO 98/45704; 1998; cited in IDS).

The instant claims recite "A method for determining the function or effect of a genetic element or a chemical modulator from a library of said genetic elements and chemical modulators having known and unknown function on a population of cells comprising: i) determining the distribution of an indicator nucleic acid sequence being expressed in said cells in the presence and the absence of a first chemical modulator or first genetic element, which modulator or genetic element affects said distribution of said indicator, wherein the cells are both co-expressing an effector nucleic acid sequence and are in the presence of a second chemical modulator or second genetic element; and ii) analysing the distribution data from all combinations of said effector, modulator or genetic element and indicator to derive functional linkages and assign function to the effector and said second modulator or second genetic element."

Thastrup et al, throughout the publication, teach methods of using various genetic materials, compounds and cells to assay for molecular functions inside cells. (e.g. Abstract).

For claims 1 and **2**: The preamble of the instant claim only recites intended use of the claimed method and does not provide additional structural limitations. See MPEP 2111.02.

The reference teaches inserting a DNA molecule encoding for a fusion protein comprising "GFP" and another protein (such as a protein kinase) into cells (e.g. Examples; pp.34+), which the GFP encoding DNA reads on the "indicator nucleic acid" as the term is broadly defined in the instant specification (p.7). The portion of the DNA that encodes for other protein (such as the protein kinase) of the fusion protein read on the "effector nucleic acid sequence" as the term is broadly defined in the instant specification (p.7). The reference also teaches testing the cells in the presence and absence of at least two other molecules including "forskolin" and "norepinephrine" (e.g. p.35, lines 4+), which the "forskolin" reads on "a first chemical modulator" and the "norepinephrine" reads on "a second chemical modulator" as the term "modulator" is broadly defined in the instant specification (p.7).

The reference also teaches detecting the cellular localization of the GFP signals (e.g. p.35, lines 6+), which reads on the "determining the distribution of an indicator nucleic acid sequence being expressed in said cells" as recited in step i) of **clms 1** and **2**.

The reference also teaches analyzing the distribution data and assessing the "stimulatory" effects of either forskolin or norepinephrine (e.g. p.35; Figure 3H). The reference also teaches the function of the protein kinase (i.e. the "effector") by measuring the amount cAMP (e.g. p.35, lines 10+), and thus assigning kinase function of the protein kinase. Therefore, the reference's teachings read on step ii) of **clm 1** and step (iii) of **clm 2**.

For claim 2: The reference also teaches measuring the "distribution" or localization of the GFP signal in cells before and after addition (or stimulation) of compounds (such as

forskolin, norepinephrine, and carbachol) using digital imaging system (e.g. pp.35-36; Figures 3, 7 and 8). The reference teaches comparing the distribution data with stimulation to without stimulation (read on known distribution data) using graphic representations, and digital imaging (e.g. pp.35+), which the both graphic and digital imaging read on electronic or optical database of **clm 2.**

For claim 3: The DNA that encodes for other protein (such as the protein kinase) of the fusion protein read on the "effector nucleic acid sequence" as the term is broadly defined in the instant specification (p.7).

For claim 4: The reference teaches transfecting plasmid containing nucleic acids encoding for a fusion protein (e.g. p.31, lines 1+), which the transfected plasmid (containing double stranded DNA) inherently comprises "an antisense oligonucleotide". An antisense oligonucleotide is the complementary strand of the sense stand (see attached Definition for Antisense downloaded from Merriam-Webster Online Dictionary on 5/8/08). That is any portion (such as a 20 nucleotide portion) of the complementary strand in the plasmid encoding for a protein (such as the protein kinase) read on "an antisense oligonucleotide", because the complementary strand would be "complementary to a segment of genetic material" (i.e. complementary to the sense strand, for example).

For claim 6: The reference teaches expression vectors comprising DNA encoding for the fusion proteins (e.g. pp.30-31).

For claim 7: The reference teaches plasmid expression vectors containing the fusion protein (e.g. pp.30-31).

For claim 8: The reference teaches using GFP (green fluorescent protein) and detecting the fluorescent signals (e.g. pp.36-37), which the GFP reads on a detectable label.

For claim 9: The reference teaches inserting a DNA molecule encoding for a fusion protein comprising "GFP" (reads on the "indicator") and another protein (such as a protein kinase) (reads on the "effector") into cells (e.g. Examples; pp.34+).

For claim 10: The reference teaches using GFP (green fluorescent protein) and detecting the fluorescent signals (e.g. pp.36-37).

For claim 11: The reference teaches using mutant GFP with at least a S65T mutation (e.g. p.30, lines 11+; p.7).

For claim 14: The reference teaches various compounds such as forskolin, norepinephrine, and carbachol (e.g. read on organic compounds) that are added to the cells (e.g. pp.35-36).

For claim 15: The recitation of "is selected from a combinatorial library…" does not provide additional structural limitation on the claimed "modulator". At best, the said recitation is a product-by-process limitation. The compounds of the reference are structurally the same as the "modulators" of the instant claims without evidence to the contrary.

For claim 16: The reference teaches using various cells such as Chinese hamster ovary cells (e.g. p.31, lines 7+), which reads on the eukaryotic cells.

For claim 17: The reference teaches using various cells such as Chinese hamster ovary cells (e.g. p.31, lines 7+) as well as mammalian cells (e.g. pp.5+).

For claim 18: The reference also teaches using cells such as "HUVEC" (human umbilical vein endothelial cells) (e.g. p.22, lines 24+), which reads on the human cells.

For claim 19: The reference teaches using digital imaging system (e.g. pp.35-36; Figures 3, 7 and 8).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Thastrup and Bastiaens

13. Claims **1-4, 6-12** and **14-19** are rejected under 35 U.S.C. **103(a)** as being unpatentable over **Thastrup** et al (WO 98/45704; 1998; cited in IDS), in view of **Bastiaens** et al. (WO 00/08054; 2/17/2000).

Thastrup et al, throughout the publication, teach methods of using various genetic materials, compounds and cells to assay for molecular functions inside cells, as discussed supra.

Thastrup et al do not explicitly teach the modified GFP has three mutations as recited in **clm 12**.

However, Bastiaens et al, throughout the publication, teach various GFP mutants (e.g. Abstract). The reference teaches a GFP mutant (e.g. "YFP5" or "MmGFP5") with mutations including F64L, S65T and S175G (e.g. p.20, Table 1), which read on the GFP mutant as recited in **clm 12**. The reference also teaches the advantages of such GFP mutants including providing a mutant with fluorescent at a unique wavelength (i.e. a red-shifted mutant) (e.g. p.17, lines 1+), longer lifetime, and provides a fluorescent label for multi-labelling experiments (e.g. p.19, lines 5+).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use a GFP mutant with the F64L, S65T and S175G mutations for signaling indicator.

A person of ordinary skill in the art would have been motivated at the time of the invention to use a mutant GFP with F64L, S65T and S175G mutations in a screening assay in cells, because Bastiaens et al teaches the advantages of such GFP mutants including providing a mutant with fluorescent at a unique wavelength (i.e. a red-shifted mutant) (e.g. p.17, lines 1+), longer lifetime, and provides a fluorescent label for multi-labelling experiments. Because both of the Thastrup and the Bastiaens references teach methods of expressing GFP mutant proteins, it would have been obvious to one skilled in the art to substitute one GFP mutant for the other to achieve the predictable result of expressing GFP mutants for detecting fluorescent signals.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since both Thastrup and Bastiaens references have demonstrated the success of using various GFP mutants for cellular screening assays.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sue Liu/
Patent Examiner, AU 1639
5/8/08